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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,765	08/21/2003	Craig A. Rosen	PS736	7999

22195 7590 09/05/2007

HUMAN GENOME SCIENCES INC.
INTELLECTUAL PROPERTY DEPT.
14200 SHADY GROVE ROAD
ROCKVILLE, MD 20850

EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	**PAPER NUMBER**
1647	

MAIL DATE	DELIVERY MODE
09/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/644,765	ROSEN ET AL.	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2006 and 31 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-41* is/are pending in the application.

4a) Of the above claim(s) *37-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *24-41* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/16/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence Alignments*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group II, drawn to polypeptides (new claims 24-36) in the reply filed on 16 August 2006 is acknowledged. Applicant has further elected HLWB056 (SEQ ID NO:180) as the one polypeptide sequence. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP §818.03(a)).

2. Claims 37-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. With regard to newly added claims 37-41, it is noted that claims 37 and 38 correspond to Group I, claim 39 corresponds to Group IV, claim 40 corresponds to Group VI, and claim 41 corresponds to Group VII of the restriction requirement (mailed 17 May 2006). The Examiner acknowledges the request for rejoinder of claims 39-41 upon the allowability of product claims 24 and/or 31. Election was made **without** traverse in the reply filed on 16 August 2006.

3. The restriction requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, and/or Claims

4. The Amendments filed on 16 August 2006 and 31 August 2006 have been entered in full. Claims 1-23 have been cancelled, claims 24-41 have been added, and claims 37-41 have been withdrawn from further consideration as discussed above. Therefore, claims 21-41 are pending, and claims 24-36 are the subject of this Office Action.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 16 August 2006 has been considered by the Examiner.

Inventorship

6. The request for the deletion of an inventor in this nonprovisional application under 37 CFR 1.48(b) is deficient because:

It lacks the required fee under 37 CFR 1.17(i).

Specification

7. The disclosure is objected to because of the following informalities:

8. The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. See for example, pg 63, line 6, pg 76, line 3, and pg 103, line 24. Applicant is required to delete the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01. Appropriate correction is suggested.

9. The use of the trademarks has been noted throughout the Specification (See pg 60, line 13, pg 85, line 22, and pg 350, line 29, for example). Trademarks should be capitalized wherever they appear and should be accompanied by the generic terminology. Applicant is encouraged to review and make appropriate corrections to the specification regarding the misuse of trademarks. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in

any manner that might adversely affect their validity as trademarks. Appropriate correction is suggested.

Claim Rejections - 35 USC § 101 and 35 USC §112, 1st Paragraph

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.
>
> The following is a quotation of the first paragraph of 35 U.S.C. 112:
>
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 24-36 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Novel biological molecules lack an established utility and must undergo extensive experimentation to determine an appropriate specific and substantial utility.

12. Specifically, claims 24-36 are directed to an isolated polypeptide comprising an amino acid sequence having at least 95% amino acid sequence identity to (a) a polypeptide comprising amino acid residues 1 to 264 of SEQ ID NO:180, (b) a polypeptide comprising amino acid residues 2 to 264 of SEQ ID NO:180, (c) a polypeptide comprising amino acid residues 17 to 264 of SEQ ID NO:180, (d) a polypeptide comprising the amino acid sequence of the complete polypeptide encoded by the HLWB056 cDNA contained in ATCC Deposit No. PTA-3105, (e) a polypeptide comprising the amino acid sequence of the complete polypeptide encoded by the

HLWB056 cDNA contained in ATCC Deposit No. PTA-3105, excepting the N-terminal methionine, (f) a polypeptide comprising the amino acid sequence of the mature portion of the polypeptide encoded by the HLWB056 cDNA contained in ATCC Deposit No. PTA-3105, (g) a polypeptide comprising at lest 30 contiguous amino acid residues of amino acid residues 1 to 264 of SEQ ID NO:180, or (h) a polypeptide comprising at lest 30 contiguous amino acid residues of amino acid residues 1 to 264 of SEQ ID NO:180. The claims also recite wherein the polypeptide is glycosylated, a composition comprising the polypeptide and a pharmaceutically acceptable carrier, and wherein the polypeptide comprises a heterologous polypeptide sequence.

9. The Specification teaches that the HLWB056 gene is expressed in the following tissues/cDNA libraries: NCI_CGAP_Lu24 and to a lesser extent in NCI_CGAP_Co14; Morton Fetal Cochlea; Stratagene ovarian cancer (#937219); NCI_CGAP_Kid11; Human Substantia Nigra; NCI_CGAP_GC4; Human Placenta; normalized infant brain cDNA; Soares_testis_NHT; Soares infant brain 1N1B; Prostate; NCI_CGAP_Pr23; Whole 6 Week Old Embryo; NCI_CGAP_Ut4; Human Epididymus; H Female Bladder, Adult; Human Infant Brain; NCI_CGAP_Ut1; NCI_CGAP_Pr28; NCI_CGAP_Gas4; Human adult testis, large inserts; Fetal Heart; Colon, normal; Human Placenta; NCI_CGAP_GC6; Human fetal heart, Lambda ZAP Express; NCI_CGAP_Co20; and NCI_CGAP_Sub3 (See pg 21-22). However, the instant specification does not teach any physiologic ligands or functional characteristics of the HLWB056 polypeptide set forth in SEQ ID NO:180. There is no well-established utility for a specific nucleic acid or amino acid HLWB056 sequence, and the specification fails to disclose a specific and substantial utility for the claimed invention. The instant application does not disclose a specific biological role for the HLWB056 protein or its significance to a particular

disease, disorder, or physiological process which one would manipulate for a desired physiological or clinical effect.

10. Based on tissue distribution, the specification asserts the following as patentable utilities for the claimed HLWB056 polypeptides:

a.) The diagnosis, prevention, and/or treatment of immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation) (See pg 22, lines 4-9); and

b.) The diagnosis, prevention, and/or treatment of cancer and other hyperproliferative disorders (See pg 22, lines 10-13).

11. These asserted utilities are neither specific nor substantial because they do not identify or reasonably confirm a "real world" context of use. The specification neither identifies the biological functions of the claimed HLWB056 protein, nor any diseases that are associated with the claimed molecules. Moreover, there does not appear to be sufficeint evidence to support the assertion that the HLWB056 polypeptides of the instant invention are associated in any way with the plurality of causally unrelated disorders that are listed on page 22 of the instant specification, including various immune system disorders; particularly immune cell proliferative disorders (e.g. leukemia), autoimmune disorders, and immunodeficiencies (including immunodeficiencies caused by genetic factors, microbial pathogens (e.g. HIV), chemotherapy, and radiation), cancer, and other hyperproliferative disorders. Without any biological activity or link to a disease, such

constitutes further research to determine the properties of the claimed HLWB056 protein, which is insufficient to meet the requirement of 35 USC § 101.

12. Utility must be in readily available form. It is possible that, after further characterization, this nucleic acid and the encoded protein might be found to have a patentable utility, in which case the proteins would have a specific utility, or the protein might be found to be associated with a specific disease or disorder. This further characterization, however, is part of the act of invention, and until it has been undertaken, Applicant's claimed invention is incomplete. Because the instant specification has failed to identify a physiological process which has been shown to be influenced by the HLWB056 protein of the instant invention, an artisan would have no way of predicting what effects the administration of that protein to an organism would have. If one cannot predict the effects that the administration of the HLWB056 protein of the instant invention is going to have on an organism, then it is unclear as to what practical or real world benefit is derived by the public from the identification of protein.

13. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sup. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which

requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

In the Instant case, the instant specification leaves it to the practitioner to discover the identity of a disease or disorder in which the protein of the instant invention is mutated or aberrantly expressed, and to discover the nature of that aberrant expression (i.e., overexpression or underexpression). The evidence of mere expression in a tissue or a cell line is not tantamount to a showing of a role of the encoded polypeptide of SEQ ID NO:180 in a disease/disorder, or that the polypeptides are useful in the diagnosis, prevention, and/or treatment of a disease or disorder. Therefore, the claimed protein cannot be used in a therapeutic capacity without the need for a substantial inventive contribution. Such additional experimentation, if needed to identify a specific utility for an invention, is precluded by the court.

15. Claims 24-36 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to make/use the claimed invention.

Claim Rejections - 35 USC § 112, 1st Paragraph (Scope of Enablement)

16. However, even if the claimed invention is eventually deemed to have a credible, specific and substantial asserted utility or a well established utility, claims 24-30 would remain rejected under 35 U.S.C. § 112, first paragraph because the instant disclosure would not be found to be enabling for the full scope of the claimed invention.

17. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

18. The claims are drawn quite broadly to an isolated polypeptide comprising an amino acid sequence having at least 95% amino acid sequence identity to (a) a polypeptide comprising amino acid residues 1 to 264 of SEQ ID NO:180, (b) a polypeptide comprising amino acid residues 2 to 264 of SEQ ID NO:180, (c) a polypeptide comprising amino acid residues 17 to 264 of SEQ ID NO:180, (d) a polypeptide comprising the amino acid sequence of the complete polypeptide encoded by the HLWB056 cDNA contained in ATCC Deposit No. PTA-3105, (e) a polypeptide comprising the amino acid sequence of the complete polypeptide encoded by the HLWB056 cDNA contained in ATCC Deposit No. PTA-3105, excepting the N-terminal methionine, (f) a polypeptide comprising the amino acid sequence of the mature portion of the polypeptide encoded by the HLWB056 cDNA contained in ATCC Deposit No. PTA-3105, (g) a polypeptide comprising at lest 30 contiguous amino acid residues of amino acid residues 1 to 264

of SEQ ID NO:180, or (h) a polypeptide comprising at lest 30 contiguous amino acid residues of amino acid residues 1 to 264 of SEQ ID NO:180. The claims also recite wherein the polypeptide is glycosylated, a composition comprising the polypeptide and a pharmaceutically acceptable carrier, and wherein the polypeptide comprises a heterologous polypeptide sequence. However, other than the HLWB056 polypeptide of SEQ ID NO:180, the disclosure fails to provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. The disclosure has not shown (1) which portions of the protein of SEQ ID NO:180 are critical to the activity of the protein of SEQ ID NO:180 (which is itself unknown); (2) what modifications e.g., substitutions, deletions, or additions) one can make to SEQ ID NO:180 that will result in protein mutants or variants with the same function/activity as the protein of SEQ ID NO:180; and (3) any guidance on how to use the variants of SEQ ID NO:180 which would, based on the language of said claims, encompass both active and inactive variants, especially in the absence of any functional limitations in the claims. The state of the art is such that the relationship between the sequence of a protein and its activity is not well understood and unpredictable, and that certain positions in the sequence are critical to the protein's structure/function relationship and can only tolerate only relatively conservative substitutions or no substitutions.

19. The problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions

in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions and still retain the activity of the protein of SEQ ID NO:180.

20. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Biological Deposits

21. Claims 24, 27, 29-30, 31, and 35-36 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

22. The deposit of biological organisms is considered by the Examiner to be necessary for enablement of the current invention (see 37 C.F.R.§1.808(a)). Examiner acknowledges the deposit of organisms under accession number PTA-3105 under terms of the Budapest Treaty on International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure in partial compliance with this requirement. However, it appears from the data presented in Table 1 that Deposit No. 3105 contains multiple different clones corresponding to multiple different genes. Therefore, the plasmid containing the cDNA encoding SEQ ID NO:180 cannot be assumed to be stable, nor necessarily maintained, in a multiply transformed cell line and thus, the Examiner cannot determine with reasonable certainty the availability of the clone encoding SEQ ID NO:180. Furthermore, in order to be fully compliant with the requirement, applicants must state that the following criteria have been met:

(a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five

(5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 C.F.R.§1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

23. In addition the identifying information set forth in 37 C.F.R.§1.809(d) should be added to the specification. See 37 C.F.R.§ 1.803-1.809 for additional explanation of these requirements.

Claim Rejections - 35 USC § 112, 1st Paragraph (Written Description)

24. Claims 24-31 and 35-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

25. Claims 24-30 are drawn quite broadly to an isolated polypeptide comprising an amino acid sequence having at least 95% amino acid sequence identity to (a) a polypeptide comprising amino acid residues 1 to 264 of SEQ ID NO:180, (b) a polypeptide comprising amino acid residues 2 to 264 of SEQ ID NO:180, (c) a polypeptide comprising amino acid residues 17 to 264 of SEQ ID NO:180, (d) a polypeptide comprising the amino acid sequence of the complete polypeptide encoded by the HLWB056 cDNA contained in ATCC Deposit No. PTA-3105, (e) a polypeptide comprising the amino acid sequence of the complete polypeptide encoded by the

HLWB056 cDNA contained in ATCC Deposit No. PTA-3105, excepting the N-terminal methionine, (f) a polypeptide comprising the amino acid sequence of the mature portion of the polypeptide encoded by the HLWB056 cDNA contained in ATCC Deposit No. PTA-3105, (g) a polypeptide comprising at lest 30 contiguous amino acid residues of amino acid residues 1 to 264 of SEQ ID NO:180, or (h) a polypeptide comprising at lest 30 contiguous amino acid residues of amino acid residues 1 to 264 of SEQ ID NO:180. The claims also recite wherein the polypeptide is glycosylated, a composition comprising the polypeptide and a pharmaceutically acceptable carrier, and wherein the polypeptide comprises a heterologous polypeptide sequence. Furthermore, claims 24 and 31 subpart (f) recite the mature portion of the polypeptide encoded by the HLWB056 cDNA contained in ATCC Deposit No. PTA-3105. Thus, the claims are drawn to a genus of polypeptide molecules that are defined only by a partial structure.

26. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Furthermore, claims 24 and 31 subpart (f) recite the mature portion of the polypeptide encoded by the HLWB056 cDNA contained in ATCC Deposit No. PTA-3105. The Specification does not disclose the specific sequence of the mature portion of the recited polypeptide. The full-length polypeptide has the sequence of SEQ ID NO:180 as disclosed in the Specification, which is not

equivalent to the specific mature portion of the polypeptide as recited in the claims. While the art acknowledges that leader/signal sequences are readily identifiable, the art also recognizes that for many proteins, full-length proteins may be processed into more than one unique compound. For example, Creighton (Proteins: Structures and Molecular Principles, 1984) teaches pro-opiomelanocortin is cleaved during processing which results in 8 different functional peptides (See pg 71, Fig. 2-6) and the mature forms may also differ by the deletion of internal amino acid residues (See pg 72, Fig. 2-7). Ganong (Review of Medical Physiology 17th Ed., 1995) teaches that prepro-oxypysin undergoes processing to form two completely different peptides, oxytocin and neurophysin I (See pg 220), and prepro-cholecystokinin-pancreozymin (CCK) undergoes multiple processing steps to produce multiple peptide fragments (See pg 446). However, the instant specification fails to provide sufficient detailed information such that one skilled in the art would be able to envision the detailed chemical structure of the "mature portion" of the polypeptide. Other than the full-length protein set forth in SEQ ID NO:180 lacking the N-terminal methionine, lacking the signal sequence, or wherein the polypeptide is glycosylated, the Specification fails to describe any "mature portion" of the polypeptide of SEQ ID NO:180.

27. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Additionally, the description of one polypeptide species (SEQ ID NO:180) is not adequate written description of an entire genus of functionally equivalent polypeptides, which incorporate all variants, derivatives, and homologs encompassed by the claims.

28. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was

in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

29. With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

30. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

31. Therefore, only an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:180 and the recited fragments thereof, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112, 2nd Paragraph

32. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

33. Claims 24-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

34. Claims 24 and 31 are rejected as being indefinite for reciting "a mature portion of the polypeptide" in part (f) of each of the claims. Does it refer to the polypeptide of SEQ ID NO:180 lacking the signal sequence (See pg 307, lines 5-11; Table 1A), or does it refer to a an unspecified form of the secreted polypeptide after it has undergone some form of extracellular processing (see pg 77, lines 9-11). Since neither the art nor the specification provides an unambiguous definition of the term, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

35. Claims 25-30 and 32-36 are rejected for depending from an indefinite claim.

Priority

36. The instant specification fails to provide a disclosure meeting the requirements of 35 U.S.C. § 101 and § 112, first paragraph. Accordingly, the claim for priority to any parent application is denied. The instant filing date, 21 August 2003, is thus used for the purposes of applying the prior art below.

Claim Rejections - 35 USC § 102

37. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

38. Claims 24-31 and 34-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Pan et al. (WO 00/69885, published 23 November 2000).

39. Pan et al. teach an isolated TANGO204 polypeptide (SEQ ID NO:2) that shares 99.2% sequence identity to SEQ ID NO:180 of the instant Application (See attached sequence alignment), as well as compositions comprising the polypeptide along with a pharmaceutical carrier (See pg 104, lines 2-12). Pan et al. also teach said polypeptide lacking the N-terminal methionine (SEQ ID NO:81); pg 32, lines 19-24), as well as a mature form of the polypeptide which comprises the polypeptide of SEQ ID NO:2 lacking the signal sequence (See SEQ ID NO:23; pg 32, lines 25-29). It is noted that the Examiner has interpreted the limitation "the mature portion of the polypeptide" as reading on the full-length polypeptide lacking the signal sequence, i.e., amino acid residues 1 to 16 of SEQ ID NO:180 (See pg 307, lines 5-11; Table 1A). The instant specification indicates that the amino acid sequence of the polypeptide encoded by the HLWB056 cDNA contained in ATCC accession number PTA-3105 is SEQ ID NO:180, and thus Pan et al. anticipates claim 24, subparts (d), (e), and (f) and claim 27. Since Pan et al. disclose that the polypeptide of SEQ ID NO:2 has a glycosylation site (See pg 33, lines 9-11) as well as the recombinant expression of said polypeptide in a eukaryotic host cell (See pg 96, lines

28-31), the polypeptide would inherently be glycosylated. Lastly, Pan et al. teach said polypeptide further comprising a heterologous polypeptide sequence (See pg 81, line 24 through pg 82, line 3). Thus, the reference of Pan et al. meets all the limitations of claims 24-31 and 34-36.

40. Claims 24-28 and 31-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Wistow et al. (Molec. Vis. 8:205-220, 19 June 2002).

41. Wistow et al. teach an isolated polypeptide that comprises an amino acid sequence (See Figure 8 at pg 214, pg 216, 1st Paragraph) that shares 100% sequence identity to SEQ ID NO:180 of the instant Application (See attached sequence alignment). The instant specification indicates that the amino acid sequence of the polypeptide encoded by the HLWB056 cDNA contained in ATCC accession number PTA-3105 is SEQ ID NO:180, and thus Wistow et al. anticipates claims 24 and 31, subparts (d), (e), and (f) and claim 27. It is further noted that the Examiner has interpreted the limitation "the mature portion of the polypeptide" as reading on the full-length polypeptide lacking the signal sequence, i.e., amino acid residues 1 to 16 of SEQ ID NO:180 (See pg 307, lines 5-11; Table 1A). Thus, the reference of Wistow et al. meets all the limitations of claims 24-28 and 31-34.

Summary

42. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 7:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Manjunath N. Rao**, can be reached on **(571) 272-0939**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Jon M. Lockard, Ph.D.
August 31, 2007

```
RESULT 1
Q96J64_HUMAN
ID   Q96J64_HUMAN   PRELIMINARY;   PRT;   298 AA.
AC   Q96J64;
DT   01-DEC-2001, integrated into UniProtKB/TrEMBL.
DT   01-DEC-2001, sequence version 1.
DT   30-MAY-2006, entry version 15.
DE   RPE-spondin (Fragment).
GN   Name=RPESP;
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
OC   Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   NUCLEOTIDE SEQUENCE.
RC   TISSUE=RPE/choroid;
RX   MEDLINE=22103460; PubMed=12107410;
RA   Wistow G., Bernstein S.L., Wyatt M.K., Fariss R.N., Behal A.,
RA   Touchman J.W., Bouffard G., Smith D., Peterson K.;
RT   "Expressed sequence tag analysis of human RPE/choroid for the NEIBank
RT   project: over 6000 non-redundant transcripts, novel genes and splice
RT   variants.";
RL   Mol. Vis. 8:205-220(2002).
CC   ---------------------------------------------------------------------
CC   Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   ---------------------------------------------------------------------
DR   EMBL; AY040546; AAK83466.1; -; mRNA.
DR   Ensembl; ENSG00000164764; Homo sapiens.
DR   LinkHub; Q96J64; -.
DR   InterPro; IPR001212; Somatomedin_B.
DR   InterPro; IPR000884; TSP1.
DR   InterPro; IPR008197; WAP.
DR   PRINTS; PR00003; 4DISULPHCORE.
DR   PRINTS; PR00022; SOMATOMEDINB.
DR   SMART; SM00209; TSP1; 1.
DR   PROSITE; PS00524; SMB_1; 1.
DR   PROSITE; PS50958; SMB_2; 1.
DR   PROSITE; PS50092; TSP1; 1.
FT   NON_TER       1      1
SQ   SEQUENCE   298 AA;  32729 MW;  EF4C9CFA9CB12D35 CRC64;

  Query Match           100.0%;  Score 1529;  DB 2;  Length 298;
  Best Local Similarity  100.0%;  Pred. No. 2.1e-119;
  Matches  264;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MRTLWMALCALSRLWPGAQAGCAEAGRCCPGRDPACFARGWRLDRVYGTCFCDQACRLTG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         35 MRTLWMALCALSRLWPGAQAGCAEAGRCCPGRDPACFARGWRLDRVYGTCFCDQACRLTG 94

Qy         61 DCCFDYDRACPARPCFVGEWSPWSGCADQCKPTTRVRRRSVQQEPQNGGAPCPPLEERAG 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
```

```
Db         95 DCCFDYDRACPARPCFVGEWSPWSGCADQCKPTTRVRRRSVQQEPQNGGAPCPPLEERAG 154

Qy        121 CLEYSTPQGQDCGHTYVPAFITTSAFNKERTRQATSPHWSTHTEDAGYCMEFKTESLTPH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        155 CLEYSTPQGQDCGHTYVPAFITTSAFNKERTRQATSPHWSTHTEDAGYCMEFKTESLTPH 214

Qy        181 CALENRPLTRWMQYLREGYTVCVDCQPPAMNSVSLRCSGDGLDSDGNQTLHWQAIGNPRC 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        215 CALENRPLTRWMQYLREGYTVCVDCQPPAMNSVSLRCSGDGLDSDGNQTLHWQAIGNPRC 274

Qy        241 QGTWKKVRRVDQCSCPAVHSFIFI 264
              ||||||||||||||||||||||||
Db        275 QGTWKKVRRVDQCSCPAVHSFIFI 298
```

RESULT 3
AAB48105
ID AAB48105 standard; protein; 264 AA.
XX
AC AAB48105;
XX
DT 02-APR-2001 (first entry)
XX
DE Human TANGO 204 polypeptide.
XX
KW TANGO 204; TANGO 206; TANGO 209; A236; secreted protein; human; mouse;
KW transmembrane protein; antianemic; cerebroprotective; arteriosclerosis;
KW antiasthmatic; neuroprotective, cytostatic; cardiant; hepatotropic;
KW antiinflammatory; antidiabetic; antiinfertility; antipyretic; vasotropic;
KW antirheumatic; nephrotropic; hemostatic; antilipemic; osteopathic;
KW ophthalmological; antisickling; antiulcer; vulnerary.
XX
OS Homo sapiens.
XX
PN WO200069885-A2.
XX
PD 23-NOV-2000.
XX
PF 15-MAY-2000; 2000WO-US013361.
XX
PR 14-MAY-1999; 99US-00312359.
XX
PA (MILL-) MILLENNIUM PHARM INC.
XX
PI Pan Y, Leiby KR;
XX
DR WPI; 2001-024999/03.
DR N-PSDB; AAC84377, AAC84378.
XX
PT Novel nucleic acids encoding secreted or transmembrane proteins, useful
PT for treating, e.g. cancer, hemophilia, anemia, ischemia or diseases of
PT the lung, liver, kidney or pancreas.
XX
PS Claim 8; Fig 1A-D; 209pp; English.
XX
CC The invention provides human and mouse nucleic acids designated TANGO
CC 204, TANGO 206, TANGO 209 and A236 encoding secreted or transmembrane
CC proteins. The polypeptides, nucleic acids and their modulators may be
CC useful for treating or modulating cholesterol uptake, blood coagulation,
CC to modulate cell proliferation, morphogenesis and fate specification,
CC tissue repair and renewal, to treat cancer and promote wound healing,
CC modulate angiogenesis, treat hypercholesterolemia, hemophilia, Marfan
CC syndrome, protein S deficiency, modulate allergic or inflammatory
CC response, acid secretion, tropic effects on gastrointestinal mucosa, and
CC promote ulcer healing, treat bone cancer, achandroplasia, myeloma,
CC fibrous dysplasia, scoliosis, osteoarthritis, osteosarcoma, osteoporosis,
CC leukemia, anemia, thalassemia, cerebral edema, hydrocephalus, brain
CC herniations, meningitis, ischemic brain or heart disease, infarction,
CC intracranial hemorage, pancreatitis, diabetes, angina, hypotensive heart
CC disease, pulmonary heart disease, rheumatic fever, congenital heart
CC disease, myocardial disease, atherosclerosis, hypertension, jaundice,
CC hepatic failure, cirrhosis, glomerulonephritis, Goodpasture's syndrome,

CC sickle cell disease, renal failure, ischemic bowel disease, Crohn's
CC disease, hernias, hypoadrenalism, hyperadrenalism, Cushing's syndrome,
CC neoplasia, pulmonary disorders, asthma, ovarian disorders, McCune
CC Albright syndrome, infertility, uterine disorders, viral disease. The
CC present sequence represents the human TANGO 204 polypeptide
XX
SQ Sequence 264 AA;

Query Match 99.2%; Score 1517; DB 4; Length 264;
Best Local Similarity 99.2%; Pred. No. 9.7e-113;
Matches 262; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

```
Qy          1 MRTLWMALCALSRLWPGAQAGCAEAGRCCPGRDPACFARGWRLDRVYGTCFCDQACRLTG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| ||
Db          1 MRTLWMALCALSRLWPGAQAGCAEAGRCCPGRDPACFARGWRLDRVYGTCFCDQACRFTG 60

Qy         61 DCCFDYDRACPARPCFVGEWSPWSGCADQCKPTTRVRRRSVQQEPQNGGAPCPPLEERAG 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 DCCFDYDRACPARPCFVGEWSPWSGCADQCKPTTRVRRRSVQQEPQNGGAPCPPLEERAG 120

Qy        121 CLEYSTPQGQDCGHTYVPAFITTSAFNKERTRQATSPHWSTHTEDAGYCMEFKTESLTPH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 CLEYSTPQGQDCGHTYVPAFITTSAFNKERTRQATSPHWSTHTEDAGYCMEFKTESLTPH 180

Qy        181 CALENRPLTRWMQYLREGYTVCVDCQPPAMNSVSLRCSGDGLDSDGNQTLHWQAIGNPRC 240
              ||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 CALENWPLTRWMQYLREGYTVCVDCQPPAMNSVSLRCSGDGLDSDGNQTLHWQAIGNPRC 240

Qy        241 QGTWKKVRRVDQCSCPAVHSFIFI 264
              ||||||||||||||||||||||||
Db        241 QGTWKKVRRVDQCSCPAVHSFIFI 264
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